UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,833	07/20/2006	Roman J. Giger	20724-011US1	3920

26167 7590 07/23/2008

FISH & RICHARDSON P.C.
P.O BOX 1022
Minneapolis, MN 55440-1022

EXAMINER	
WOODWARD, CHERIE MICHELLE	
ART UNIT	PAPER NUMBER
1647	
MAIL DATE	DELIVERY MODE
07/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,833	GIGER, ROMAN J.	
	Examiner	Art Unit	
	CHERIE M. WOODWARD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35,38-51 and 62-74* is/are pending in the application.

4a) Of the above claim(s) *1-35,42-49 and 62-74* is/are withdrawn from consideration.

5)☒ Claim(s) *38-41* is/are allowed.

6)☒ Claim(s) *50 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3 October 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Applicant's Response and Amendments to the claims and the specification, filed on 28 April 2008, is acknowledged and entered. Claims 36-37 and 52-61 have been cancelled by Applicant. Claims 1-35, 42-49, and 62-74 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 38-41 and 50-51 are under examination.

Response to Arguments

Objections/Rejections Withdrawn

2. The objection to the drawings is withdrawn in light of Applicant's amendments to the Brief Description of the Drawings in the specification.

3. The objection to the disclosure is withdrawn in light of Applicant's amendments to the Brief Description of the Drawings in the specification.

4. The objection to claim 39 is objected to under 37 CFR 1.821(d) is withdrawn in light of Applicant's clarification in the Remarks, filed 4/28/2008, at page 11, third and fourth paragraphs.

5. The objection to claims 39 and 40 is withdrawn in light of Applicant's clarification in the Remarks, filed 4/28/2008, at page 11, third and fourth paragraphs.

6. The objection to claim 40 as being dependent upon a rejected base claim is withdrawn in light of Applicant's amendments.

7. The rejection of claim 40 under 35 U.S.C. 112, second paragraph, is withdrawn in light of Applicant's amendments.

8. The rejection of claims 38, 39, and 41 under 35 U.S.C. 112, first paragraph, written description, is withdrawn in light of Applicant's amendments.

9. The rejection of claims 38, 39, and 41 under 35 U.S.C. 112, first paragraph, scope of enablement, is withdrawn in light of Applicant's amendments.

Claim Rejections Maintained

Claim Rejections - 35 USC § 112, First Paragraph

Scope of Enablement

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 50 and 51 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for decreasing myelin inhibitor activity, does not reasonably provide enablement for the full scope of "modulating" myelin inhibitor activity or treating the claimed genera of central nervous system disorders, for the reasons of record and the reasons set forth herein.

Applicant argues that the claims are enabled (Remarks, page 132, second paragraph). However, Applicant sufficiently explains the conflict between the Barton reference and the specification (Remarks, p. 12, third paragraph). Applicant does not specifically address the issues related to claims 50 and 51 (Remarks, page 13, first paragraph; see especially Remarks, p. 14, third paragraph)). Applicant's amendments do overcome some parts of the initial scope of enablement rejection related to the "MAG binding domain." However, significant issues remain and claims 38, 39, 41, 50 and 51 remain rejected. Applicant's arguments are not entirely persuasive for the reasons set forth below.

Amended claim 38 recites a chimeric NgR1 protein comprising residues 315-327 of NgR2 and the ligand binding domain of NgR1. In the absence of an alternative definition, an "NgR1 protein" reads on the whole protein and not a fragment thereof. Claim 38 is written in such a way that it literally recites the whole NgR1 protein also comprising residues 315-327 of NgR2 and the ligand binding domain of NgR1 (which the specification teaches as residues 1-314 of NgR1 at page 14, line6), As such, it would require undue experimentation for a person of skill in the art to make and test a sufficient number chimeric NgR1 fusion proteins comprising residues 315-327 of NgR2 and the ligand binding domain of NgR1 and test the same for activity. Without additional guidance, one of ordinary skill in the art would not know how to make or use "a chimeric NgR1 protein" comprising residues 315-327 of NgR2 and the ligand binding domain of NgR1 because the claim also appears to require the structure of the whole NgR1

protein. Applicant may overcome this aspect of the rejection by deleting the phrase "NgR1" from the preamble of claim 38 so that the preamble reads "[a] chimeric protein comprising…"

Claim 50 recites modulating myelin inhibitory activity comprising contacting a myelin-derived-growth inhibitory protein with the chimera of claim 38. Claim 51 recites a method of treating a central nervous system disorder in a subject comprising administering to the subject an effective amount of the chimera of claim 38. As previously stated in the Office Action of 12/31/2007, there are no working examples of *in vivo* administration or treatment of any species of central nervous system disorder using the claimed chimeric fusion proteins. Similarly the term "modulating" in claim 50 is broadly read as increasing or decreasing myelin inhibitory activity. There are no working examples of increasing myelin inhibitory activity comprising contacting a myelin-derived-inhibitory protein with the chimera of claim 38. Although working examples are not required, they are helpful in determining whether Applicant has sufficiently taught how to make and use the invention within its full scope.

He et al., (Neuron. 2003 Apr 24;38(2):177-185) (previously cited of record) teach that the failure of axon regeneration in the adult mammalian central nervous system (CNS) is at least partly due to inhibitory molecules associated with myelin (abstract). Recent studies suggest that an axon surface protein, the Nogo receptor (NgR), may play a role in this process through cross-reactivity with myelin-associated inhibitory ligands (abstract). He et al., disclose the crystal structure and functional characterization of a soluble extracellular domain of the human Nogo receptor that provides a framework for structure-function studies aimed at assessing the physiological relevance of NgR-mediated protein-protein interactions to axon regeneration inhibition (abstract). Similarly, Barton et al., (EMBO J. 2003 Jul 1;22(13):3291-3302) (previously cited of record), teach that the myelin-derived proteins Nogo, MAG and OMgp limit axonal regeneration after injury of the spinal cord and brain (abstract).

Domeniconi et al., (Neuron. 2002 Jul 18;35(2):283-90)(previously cited of record) teach myelin inhibitors of axonal regeneration, like Nogo and MAG, that block regrowth after injury to the adult CNS (abstract). MAG inhibits regeneration by interaction with NgR. Binding of and inhibition by MAG are lost if neuronal GPI-linked proteins are cleaved (abstract). Binding of MAG to NgR-expressing cells is GPI dependent and sialic acid independent (abstract). Conversely, NgR binds to MAG-expressing cells. MAG, but not a truncated MAG, binds neurons, but does not inhibit regeneration, and precipitates NgR from NgR-expressing cells and cerebellar neurons (abstract). NgR antibody, soluble NgR, or dominant-negative NgR each prevent inhibition of neurite outgrowth by MAG. Also, MAG and Nogo66 compete for binding to NgR. The results by Domeniconi et al., suggest redundancy in myelin inhibitors and indicate the potential, but unproven therapeutic value of the claimed chimera in CNS traumatic injuries

(abstract), but not necessarily "modulation" of myelin inhibitory activity, as claimed in claim 50 or treatment of the full spectrum of central nervous system disorders as claimed in claim 51.

Because neither the art nor the specification teaches treatment of any species of central nervous system disorder, which include disorders such as amyotrophic lateral sclerosis (ALS), multiple sclerosis, stroke, prion disease, and Alzheimer's disease, one of ordinary skill in the art would not be able to predictably use the method of claim 51 without undue experimentation. Additionally, the phrase "myelin-derived-growth-inhibitory protein" in claim 50 is not defined or otherwise limited in the specification. The specification discloses that the phrase includes the ligands Nogo, MAG, and OMgp (p, 16, lines 2-4). However, the recitation of only three ligands is insufficient to provide sufficient guidance on what a "myelin-derived-growth-inhibitory protein" is supposed to be. As such, one of skill in the art would not be able to predictably determine what a "myelin-derived-growth-inhibitory protein" is such that one of ordinary skill in the art could use predictably use the claimed method of "modulating" myelin inhibitory activity without undue experimentation.

Due to the large quantity of experimentation necessary to determine how to use the claimed method of "modulating" myelin inhibitory activity (which encompasses "increasing" myelin inhibitory activity), or how to use the method of treating a central nervous system disorder to treat, Alzheimer's disease, for example, the lack of direction/guidance presented in the specification regarding same, the absence of sufficient working examples directed to same, the complex nature of the invention, the state of the prior art establishing a redundancy in myelin inhibitors, and the breadth of the claims which fail to recite specific central nervous system disorders or specific myelin-derived-growth inhibitory proteins, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

It is noted that broad claims may be rejected merely because they read on a significant number of inoperative species when examiner sets forth reasonable grounds in support of his or her conclusions that the claims may read upon inoperative subject matter and it becomes incumbent upon applicant either to reasonably limit claims to approximate area where operativeness has not been challenged or to rebut examiner's challenge by submission of representative evidence or by persuasive arguments based on known laws of physics and chemistry (see *In re Cook and Merigold*, 169 USPQ 298 (CCPA 1971)).

Claim Rejections - 35 USC § 112, First Paragraph

Written Description

12. Claims 50 and 51 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for the reasons of record and the reasons set forth herein.

Applicant argues that the written description does not require a complete structure of every species within the genus (Remarks, p. 13, last paragraph). Applicant argues that the amendments are sufficient to show one of ordinary skill in the art that Applicant was in possession of the claimed genus (Remarks, p. 14, second paragraph). Applicant argues that claims 50 and 51 are adequately described, but does not specifically address the issues related to these two claims (Remarks, page 13, second paragraph to page 14, third paragraph; see especially Remarks, p. 14, third paragraph). However, significant issues remain and claims 50 and 51 remain rejected. Applicant's arguments are not persuasive for the reasons set forth below.

Claim 50 recites modulating myelin inhibitory activity comprising contacting a myelin-derived-growth inhibitory protein with the chimera of claim 38. Claim 51 recites a method of treating a central nervous system disorder in a subject comprising administering to the subject an effective amount of the chimera of claim 38.

Neither the art nor the specification adequately describe treatment of the full scope of central nervous system disorders as claimed, such that the description is sufficient to demonstrate that Applicant was in possession of the full scope of the claims. He et al., (Neuron. 2003 Apr 24;38(2):177-185) (previously cited of record) teach that the failure of axon regeneration in the adult mammalian central nervous system (CNS) is at least partly due to inhibitory molecules associated with myelin (abstract). Recent studies suggest that an axon surface protein, the Nogo receptor (NgR), may play a role in this process through crossreactivity with myelin-associated inhibitory ligands (abstract). Similarly, Barton et al., (EMBO J. 2003 Jul 1;22(13):3291-3302) (previously cited of record), teach that the myelin-derived proteins Nogo, MAG and OMgp limit axonal regeneration after injury of the spinal cord and brain (abstract). Domeniconi et al., (Neuron. 2002 Jul 18;35(2):283-90) (previously cited of record) teach myelin inhibitors of axonal regeneration, like Nogo and MAG, that block regrowth after injury to the adult CNS (abstract). MAG inhibits regeneration by interaction with NgR. Binding of and inhibition by MAG are lost if neuronal GPI-linked proteins are cleaved (abstract). Binding of MAG to NgR-expressing cells is GPI dependent and sialic acid independent (abstract). Conversely, NgR binds to MAG-expressing cells. MAG, but not a truncated MAG, binds neurons, but does not inhibit regeneration, and precipitates NgR from NgR-expressing cells and cerebellar neurons (abstract). NgR antibody, soluble NgR, or dominant-negative NgR each prevent inhibition of neurite outgrowth by MAG. Also, MAG and Nogo66 compete for binding to NgR. The results by Domeniconi et al., suggest redundancy in myelin inhibitors and describe the potential, but unproven therapeutic value of the claimed chimera in CNS traumatic

injuries (abstract), but not necessarily "modulation" of myelin inhibitory activity, as claimed in claim 50 or treatment of the full spectrum of central nervous system disorders as claimed in claim 51.

Without an adequate written description of treatment of the claimed full spectrum of central nervous system disorders, encompassing for example, amyotrophic lateral sclerosis (ALS), multiple sclerosis, stroke, prion disease, and Alzheimer's disease, Applicant has not demonstrated that they are in possession of the method of claim 51 in its full scope. Further, the term "modulating" in claim 50 is broadly read as increasing or decreasing myelin inhibitory activity. There are no working examples in the specification or the art of increasing myelin inhibitory activity comprising contacting a myelin-derived-inhibitory protein with the chimera of claim 38. While "examples explicitly covering the full scope of the claim language" typically will not be required, a sufficient number of representative species must be included to "demonstrate that the patentee possessed the full scope of the [claimed] invention." Lizardtech v. Earth Resource Mapping, Inc., 424 F.3d 1336, 1345, 76 USPQ2d 1724, 1732 (Fed. Cir. 2005). Additionally, the phrase "myelin-derived-growth-inhibitory protein" in claim 50 is not defined or otherwise limited in the specification. The specification discloses that the phrase includes the ligands Nogo, MAG, and OMgp (p, 16, lines 2-4). However, the description of only three ligands is insufficient to provide an adequate written description for a "myelin-derived-growth-inhibitory protein.". As such, Applicant has not adequately demonstrated that they are in possession of the full scope of the method of claim 50.

In the absence of sufficient recitation of distinguishing characteristics, such as species of central nervous system disorders or myelin-derived-growth-inhibitory proteins, the specification does not provide adequate written description of the claimed genus. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus. Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features (see, Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 927, 69 USPQ2d 1886, 1895 (Fed. Cir. 2004); accord Ex Parte Kubin, 2007-0819, BPAI 31 May 2007, opinion at p. 16, paragraph 1). The specification does not clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed (see *Vas-Cath* at page 1116).

Conclusion

Claim 38-41 are allowable.

Claims 50 and 51 remain rejected.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHERIE M. WOODWARD whose telephone number is (571)272-3329. The examiner can normally be reached on Monday - Friday 9:00am-5:30pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CMW/
AU 1647